DOCUMENT RESUME

ED 284 840 SP 029 027

TITLE	Immunization. Safety and Use of Polio Vaccines. Briefing Report to the Chairman, Subcommittee on Natural Resources, Agriculture Research and Environment, Committee on Science, Space, and Technology, House of Representatives.
INSTITUTION	General Accounting Office, Washington, D.C.
REPORT NO	GAO/HRD-87-83BR
PUB DATE	May 87
NOTE	15p.
AVAILABLE FROM	U.S. General Accounting Office, P.O. Box 6015, Gaithersburg, MD 20877 (First five copies are free, additional copies are $2.00 each; 25 percent discount for orders of 100 or more).
PUB TYPE	Information Analyses (070)
EDRS PRICE	MF01/PC01 Plus Postage.
DESCRIPTORS	Children; Communicable Diseases; Disease Control; Federal Legislation; *Federal Programs; Federal Regulation; *Immunization Programs
IDENTIFIERS	*Polio Vaccines

ABSTRACT

This report presents information on the status of the safety and use of polio vaccines in the United States. Topics discussed include: (1) the role of the Food and Drug Administration (FDA) in processing an inactivated polio vaccine license application; (2) the steps the federal government has taken to improve the safety of the vaccine; (3) the Immunization Practices Advisory Committee's basis for recommending the use of a live polio vaccine for routine childhood immunization; and (4) the steps required to make an inactivated polio vaccine the recomended one for children. (CB)

****
* Reproductions supplied by EDRS are the best that can be made *
* from the original document. *
****

United States General Accounting Office

GAO

Briefing Report to the Chairman, Subcommittee on Natural Resources, Agriculture Research and Environment, Committee on Science, Space, and Technology, House of Representatives

May 1987

IMMUNIZATION

Safety and Use of Polio Vaccines

ED284840

U.S. DEPARTMENT OF EDUCATION
Office of Educational Research and Improvement
EDUCATIONAL RESOURCES INFORMATION CENTER (ERIC)

☐ This document has been reproduced as received from the person or organization originating it.

☐ Minor changes have been made to improve reproduction quality.

• Points of view or opinions stated in this document do not necessarily represent official OERI position or policy.

GAO

United States
General Accounting Office
Washington, D.C. 20548

Human Resources Division

B-226814

May 11, 1987

The Honorable James H. Scheuer
Chairman, Subcommittee on Natural
Resources, Agriculture Research
and Environment
Committee on Science, Space,
and Technology
House of Representatives

Dear Mr. Chairman:

This briefing report responds to your September 8, 1986, letter in which you expressed several concerns related to polio vaccines. Specifically, you requested information on (1) the reasons the Food and Drug Administration (FDA) was slow in acting on a license application for Institut Merieux's inactivated polio vaccine; (2) the steps the federal government has taken to improve the safety of the currently used live oral polio vaccine; (3) the Immunization Practices Advisory Committee's basis for recommending the use of a live polio vaccine for routine childhood immunization; and (4) the steps required to make an inactivated polio vaccine the recommended one for children.

We reviewed records at FDA related to its processing of Merieux's inactivated polio vaccine license application; we also reviewed records at the Centers for Disease Control and the Immunization Practices Advisory Committee related to the recommendation of the live polio vaccine. We interviewed officials of several federal agencies about their actions to improve the safety of the currently used live polio vaccine, and we reviewed summaries of their research. We also interviewed officials of the Immunization Practices Advisory Committee and several private organizations concerning (1) why a live vaccine is recommended for routine childhood immunizations over the currently licensed inactivated polio vaccine and (2) the steps needed to make an inactivated vaccine the recommended polio vaccine. The Subcommittee agreed that we would not independently determine whether the federal government was taking the necessary steps to ensure a safer live vaccine because we do not have the expertise to evaluate the scientific basis of safety actions.

On January 6, 1987, we briefed your office on the results of our work. Based on our review of FDA's processing of Institut Merieux's license application (the license is still not approved), we concluded that the agency was not slow in acting on this application. Since March 1983, when Institut Merieux submitted its application, FDA has requested from Institut Merieux, at various times, information needed for application approval. FDA has waited as long as 21 months for some of the requested information.

On April 24, 1987, we provided your office with detailed information on FDA's actions on this application, which support our conclusion. As agreed with the Subcommittee, because the information concerning this application is considered commercially confidential by FDA, we do not discuss this matter in this briefing report. The results of our work on your remaining concerns are summarized below and discussed in detail in the enclosed report.

Our findings follow:

-- Four federal agencies, including FDA, are performing or funding research on polio viruses that ultimately may improve the safety of live polio vaccine. Officials of three private organizations that recommend to their members which vaccine should be used believe the current federal research efforts on the safety of the live polio vaccine are generally adequate because the risk of an adverse effect from this vaccine is low. (See p. 8.)

-- Since 1964, the Immunization Practices Advisory Committee has recommended the use of the live polio vaccine for routine childhood immunization. In October 1985, the Committee reviewed polio vaccines and recommended the continued use of the live polio vaccine because of its advantages over the currently licensed inactivated polio vaccine. For example, live polio vaccine has the ability to immunize unvaccinated people through contact, primarily families with a recently vaccinated child. (See p. 10.)

-- Several steps, such as demonstrating the efficacy and safety of an improved inactivated polio vaccine, are required before this vaccine could be recommended as the preferred polio vaccine for children. (See p. 12.)

As requested by your office, we did not obtain official agency comments on this report. However, we did obtain the views of program officials at FDA and the Centers for Disease Control. Their comments were incorporated, where appropriate, in this briefing report. Today, we are sending copies of this report to the Secretary of Health and Human Services, the Commissioner of FDA, the Director of the Centers for Disease Control, and other interested parties. We will also make copies available to others on request.

Should you wish to discuss the information provided, please call me on 275-6207.

Sincerely yours,

David P. Baine

David P. Baine
Associate Director

Table of Contents

	Page
LETTER	1
IMMUNIZATION: SAFETY AND USE OF POLIO VACCINES	5
Introduction	5
Objectives, Scope, and Methodology	7
Federal Efforts to Improve the Safety of Live Polio Vaccine	8
Immunization Practices Advisory Committee Recommends Live Polio Vaccine	10
Actions Required to Make Inactivated Polio Vaccine the Recommended Vaccine	12

ABBREVIATIONS

CDC	Centers for Disease Control
FDA	Food and Drug Administration
IPV	inactivated polio vaccine
OPV	oral polio vaccine

IMMUNIZATION:
SAFETY AND USE OF POLIO VACCINES

Because of the development of new polio vaccines and the risk of contracting vaccine-associated polio from a currently used vaccine, the Chairman, Subcommittee on Natural Resources, Agriculture Research and Environment, House Committee on Science, Space, and Technology, requested that we obtain information about these vaccines.

In the early 1950's, about 16,000 people contracted paralytic polio in the United States each year; today, through the introduction of polio vaccines, an average of only 10 persons contract paralytic polio each year. Two types of polio vaccines are used in this country: oral (live virus) and inactivated (killed virus) polio vaccines. The United States primarily uses an oral polio vaccine (OPV) to immunize children, and about 97 percent of them are immunized against polio by the time they enter school. However, about 9 of the 10 cases of paralytic polio per year are associated with this vaccine. The remaining case results from U.S. citizens who travel to foreign countries or come into contact with immigrants from countries where nonvaccine-associated polio viruses are circulating.

INTRODUCTION

Polio infections are caused by one of three polio viruses; 90 to 95 percent of all infections are without any symptoms. In another 4 to 8 percent of the infections, the symptoms are mild, such as fever, headache, or sore throat; only 0.1 percent of all infections result in paralysis. Both live and inactivated vaccines have provided full protection against paralytic polio.

Since 1964, OPV has been the vaccine recommended to the U.S. Department of Health and Human Services's Public Health Service for immunizing most children. This vaccine, developed by Dr. Albert Sabin, was licensed in the United States in 1963. It consists of the polio viruses in a live attenuated[1] form; the vaccine establishes a mild infection in the intestines, producing protective antibodies. OPV not only immunizes vaccinees but may also immunize nonvaccinated people who come into contact with them, primarily families with a recently vaccinated child. About 23 million doses of OPV are distributed annually in this

---

[1]An attenuated virus is a virus whose ability to produce disease has been weakened or diluted.

029027

country[2]. OPV, however, sometimes causes paralytic polio. About one case of vaccine-related paralytic polio occurs per 2.6 million doses of OPV distributed--about nine cases annually. OPV is also the recommended polio vaccine for children in the majority of other countries, including the United Kingdom, West Germany, Spain, and Japan.

Inactivated polio vaccine (IPV), developed by Dr. Jonas Salk, was licensed in the United States in 1955. This vaccine, consisting of polio viruses in a killed, that is, inactivated, form immunizes by producing antibodies that circulate in the bloodstream. Although in the United States this vaccine is no longer the recommended one for children, it is recommended for unvaccinated adults with an increased risk of exposure to polio and any persons with an immune-deficiency. IPV has no known adverse effect in vaccinees; however, to maintain a safe level of immunization, in addition to four doses during infancy, repeated booster shots of the currently licensed IPV are recommended at 5-year intervals until the child is 18 years old. Currently, about 40,000 doses of this IPV are distributed annually in the United States. Finland, the Netherlands, Norway, and Sweden use an inactivated vaccine for routine vaccination of children.

The Food and Drug Administration (FDA) approves the manufacture and distribution of vaccines in the United States. This agency, under the authority of the Public Health Service Act, requires a vaccine manufacturer to obtain a license for each vaccine product distributed for sale in U.S. interstate commerce.

The Centers for Disease Control (CDC) is responsible for (1) the surveillance of vaccine-preventable diseases and (2) the development and implementation of national goals to prevent and control vaccine-preventable diseases, especially in children. CDC performs and funds research on the safety, efficacy, and appropriate use of new and currently approved vaccines. The Public Health Service has delegated to CDC the responsibility for providing technical assistance to states and local health departments in operating their immunization programs.

Various parties, such as public health clinics, private doctors, and health maintenance organizations, administer vaccines to the U.S. population. The Immunization Practices

---

[2]The doses distributed are the total number of doses that manufacturers distribute to both public and private health sectors. Information on the number of doses administered to people is not available.

Advisory Committee[3] makes recommendations to CDC concerning the most appropriate vaccines to use. CDC promotes the vaccine recommendations and publishes them for use by state and local health agencies. In addition, private organizations, such as the American Academy of Pediatrics and the American College of Physicians, issue guidelines to their members on the appropriate polio vaccine to use in immunizing patients.

In addition to the efforts of FDA and CDC, there are other federal agencies that provide resources for research on polio and other infectious diseases. For example, the National Institutes of Health and the Agency for International Development perform or fund research on polio viruses or vaccines or both.

OBJECTIVES, SCOPE, AND METHODOLOGY

Our work was directed at determining

-- the steps the federal government has taken to improve the safety of OPV,

-- the basis of the Immunization Practices Advisory Committee's most recent recommendation of OPV for routine childhood immunization, and

-- the steps required to make IPV the recommended vaccine.

We obtained information from FDA, the National Institutes of Health, the Agency for International Development, and CDC about recent federal research on the polio viruses and polio vaccines. We reviewed CDC's and the Immunization Practices Advisory Committee's records relating to the recommendation of OPV. In addition, we discussed the safety of OPV and issues relating to whether IPV or OPV should be the recommended vaccine for children with officials of the following organizations: FDA, CDC, the American Academy of Pediatrics, the American Medical Association, the National Academy of Sciences, the American College of Physicians, and the American Academy of Family Physicians.

Because we do not have the expertise to evaluate the scientific basis of safety actions, we did not independently determine whether the federal government has taken the necessary steps to improve the safety of OPV. However, we obtained opinions from officials of private organizations, such as the

---

[3]This committee was previously called the Advisory Committee on Immunization Practices. Members are selected for their knowledge in the fields of immunization practices, public health, and the use of vaccines in preventive medicine. Officials of FDA and the National Institutes of Health serve as ex-officio members.

American College of Physicians and the American Academy of Pediatrics, concerning federal efforts to improve OPV's safety.

FEDERAL EFFORTS TO IMPROVE THE SAFETY OF LIVE POLIO VACCINE

Although federal efforts were not specifically directed at improving the safety of OPV, officials at four agencies, including FDA, told us that research directed at understanding polio viruses may lead to a safer vaccine. In addition, officials of three private organizations that recommend to their members the type of polio vaccine to use told us that the current amount of federal research on polio is sufficient because the risk of an adverse effect from OPV is low.

In fiscal year 1986, FDA allocated about 3 staff years to five internal projects on polio vaccines and viruses. Three projects were directed at determining the efficacy of polio vaccines. Two were general studies on the polio viruses. An FDA official said that most general research on the polio viruses is directed at obtaining a fuller understanding of the viruses and their genetic characteristics; thus, when the viruses are included in the vaccines, they will not cause polio. This type of research may lead to production of a safer OPV using genetic-engineering techniques.

An FDA official said that the agency did not fund extramural research on polio vaccines or viruses. However, FDA officials sponsored and participated in conferences at which potential improvements to the safety of OPV were discussed.

In addition, FDA has proposed changes to its OPV regulations. The purpose of these changes is to make FDA regulations consistent with current scientific knowledge and the World Health Organization requirements and to remove unnecessary regulatory burdens. An FDA official indicated that some of the changes to the safety tests required by the proposed regulations would ensure a safer OPV.

These proposed regulations include a change in manufacturing requirements for future OPVs licensed in the United States. This change would limit the number of times human cell cultures can be used in preparing OPV. Evidence suggests that repeated use of human cell cultures increases the possibility that the polio viruses in the vaccine may revert to a more neurovirulent[4] state after ingestion. The currently licensed OPV is grown solely in monkey kidney cells so that it would not be affected by this change. FDA's Vaccines and Related Biological Products Advisory

---

[4]Neurovirulence is the capability of a virus to produce an infection in the nervous system.

Committee approved the proposed regulations in January 1987 and, as of April 15, 1987, FDA was preparing responses to the comments received on this proposal.

The National Institutes of Health provided most of the federal resources for polio research, and most of these resources were directed at gaining a fuller understanding of polio viruses. During fiscal year 1986, the National Institute for Allergy and Infectious Diseases and the National Cancer Institute made grants totaling about $2.2 million for 23 projects that included polio as a segment of the research. Twenty-two of the projects were concerned with gaining a better understanding of polio viruses, which may ultimately lead to a safer vaccine. The purpose of the remaining project was to determine whether cancer is caused by several vaccines, one of which is polio.

CDC also performed and funded research on polio during fiscal year 1986. Three intramural studies were directed at gaining a better understanding of the polio viruses that may lead to an improved OPV. In addition, CDC officials said that agency scientists have performed surveys in Africa on lameness caused by polio and continue to assist in investigations of polio outbreaks in some foreign countries.

CDC is also funding two extramural studies: (1) a comparison of the U.S.-approved OPV with an unapproved, more potent IPV to determine differences in their ability to protect infants from the disease and to prevent transmission of the polio viruses to others and (2) a determination of the safety and efficacy of OPV when simultaneously administered with other vaccines.

The Agency for International Development's vaccine research program, except for the malaria vaccine, started in 1985. The agency has not performed polio research; however, four polio vaccine projects are in the developmental phase. All of these projects will evaluate the effectiveness of OPV or IPV, but are not directed toward improving OPV's safety.

Until November 1986, the Interagency Group to Monitor Vaccine Development, Production and Usage coordinated federal vaccine research activities at five agencies--FDA, CDC, the National Institutes of Health, the Department of Defense, and the Agency for International Development. These activities are now coordinated by the National Vaccine Program; the program also determines which vaccines are to be given priority. The National Childhood Vaccine Injury Act of 1986 (42 U.S.C. 201) established this program to achieve optimal prevention (1) of human infectious diseases through immunization and (2) against adverse reactions to vaccines.

Generally, officials of the private organizations that review and recommend polio vaccines told us that federal research efforts to improve the safety of OPV are adequate. For example, officials of the American College of Physicians and the American Academy of Family Physicians said that the federal government, with its limited resources, should give OPV research a low priority in its vaccine research efforts; they said this because, in comparison with other vaccines that are used to prevent infectious diseases, there is little risk from OPV.

IMMUNIZATION PRACTICES ADVISORY COMMITTEE RECOMMENDS LIVE POLIO VACCINE

Since the development of IPV and OPV about 25 years ago, there has been continuing controversy over which is the safer and more effective vaccine and which should be recommended for routine childhood immunization in this country. Proponents of IPV criticize the continuing risk of vaccine-associated polio cases from OPV. Proponents of OPV argue that IPV may not provide long-lasting immunity and, if recommended for childhood immunizations, may lead to a significant increase in the number of nonvaccine-associated paralytic polio cases. This controversy intensified following the development of improved IPVs in foreign countries.

Since 1964, the Immunization Practices Advisory Committee has recommended that OPV be used for routine childhood immunization because of its advantages over IPV. Although the Committee's recommendations for OPV were directed toward state and local health agencies, the Committee's Chairman told us that it considered the vaccine's benefits and risks to the individual as well as the benefits and risks to the whole population.

In 1985, the Committee again reviewed the polio vaccine issue and continued its recommendation of OPV. At this time, Committee members were provided with several papers from CDC, which discussed the advantages and disadvantages of vaccination with IPV and OPV, as well as with a newly developed, more potent IPV. The following major advantages were cited in these papers or considered by the Committee in recommending, for the immunization of most children, OPV over the currently licensed IPV:

-- OPV vaccinees may immunize unvaccinated people through contact. According to CDC officials, this is an especially important advantage because of the large number of U.S. immigrants coming from countries where polio exists.

-- OPV provides a higher level of intestinal immunity than IPV. Intestinal immunity helps prevent the spread of the virus through the community.

-- OPV costs less than IPV. The Committee's Chairman said that because of the limited funds of public health clinics, the Committee must consider the cost of the vaccine along with other factors in making recommendations.

-- OPV is easy to administer. During a child's first 2 years, the Committee recommends three oral doses of OPV whereas it recommends four injections of IPV. Generally, the easier a vaccine is to administer, the greater the number of people fully immunized.

-- The three doses of OPV will provide long-lasting, perhaps lifetime, immunity against polio. The Committee recommends that children given the currently licensed IPV receive boosters every 5 years until they are 18 years old.

Although the Immunization Practices Advisory Committee cannot recommend a vaccine that is not licensed in the United States, the Committee, during its October 1985 review of the polio vaccines, considered a newly developed and more potent IPV not yet licensed for use in this country. The more potent IPV has several advantages over the currently licensed IPV. The more potent IPV (1) provides a higher level of immunity so that it may require only three doses of the vaccine before the age of 2; (2) does away with the need for additional booster shots; and (3) may cost less to manufacture, because of new manufacturing techniques, than the currently licensed IPV.

A study, included in the papers CDC provided the Committee in 1985, compared the use of OPV with a more potent IPV that might be used in the United States. CDC officials developed a model that followed a hypothetical group of 3.5 million persons from birth to the age of 30. CDC officials used several assumptions, including, for each vaccine, efficacy and percentage of people vaccinated. The officials calculated the number of people who would contract paralytic polio if IPV was the preferred vaccine for childhood immunizations and the number if OPV was preferred.

The results indicated that if IPV alone was used to vaccinate children, 74 cases of polio may occur annually among those children or adults who did not receive full vaccination. Using OPV as the recommended vaccine, about 10 polio cases would continue to occur. According to the study, these results were, however, heavily dependent on the risk of exposure to polio

viruses. Although the model assumed a 95-percent vaccination rate for both IPV and OPV, fewer people would be susceptible to polio using OPV because some unimmunized people will become immunized after contact with vaccinees. The study indicated that if the exposure to the polio viruses decreases (for example, if polio was eradicated from the Americas), the benefits of OPV may diminish, and use of IPV may result in fewer cases of polio.

ACTIONS REQUIRED TO MAKE INACTIVATED POLIO VACCINE THE RECOMMENDED VACCINE

We discussed the actions that would be required to make IPV the recommended polio vaccine with officials of the following: FDA, CDC, Immunization Practices Advisory Committee, and four private organizations that recommend which polio vaccines should be used. The most frequently mentioned actions needed were

-- licensing a more potent IPV for marketing in the United States;

-- demonstrating the efficacy and safety of a more potent IPV; and

-- reducing the inadvertent importation of polio viruses into this country.

Officials also indicated other actions that would help IPV become the recommended vaccine. These improvements included lowering the cost of producing IPV and reducing the number of IPV doses recommended for full immunity.

Federal and private organization officials stated that before an IPV would be recommended for routine childhood immunization, it must exceed the excellent record of OPV. A CDC official said, "OPV has done a terrific job. We have eliminated [nonvaccine-associated paralytic] polio from the United States by the use of oral polio vaccine . . . there is a substantial reluctance to take any risk with that achievement."

After the Immunization Practices Advisory Committee's review of polio vaccines in October 1985, Committee members agreed that there was a need for more data before a major change in its recommendation would be warranted. For example, one advantage of OPV is that, as mentioned earlier, it produces intestinal immunity that sets up a barrier, through protective antibodies, against the spread of polio viruses. There is a question as to whether IPV can produce the same degree of immunity. To recommend IPV without this assurance may result in an increase in the number of nonvaccine-associated paralytic polio cases because of (1) the continued importation of polio viruses from South and Central America and (2) an increase in the spread of these

viruses in the United States. Federal and private organization officials said that polio must be reduced in South and Central America before IPV can be the recommended polio vaccine. According to FDA and CDC officials, such efforts have been started by the Pan American Health Organization, which plans to eradicate polio throughout the Americas within the next 5 years.

There must also be data to demonstrate that IPV causes fewer adverse effects than OPV. A CDC official said that his agency is uncertain as to the presence of adverse effects from IPV in small countries, but these countries cannot be compared with the United States, where there is one case of OPV vaccine-associated paralytic polio per 2.6 million doses distributed. The IPV adverse effects in small countries, whose birth rate is about 100,000 annually, might go unnoticed if the effects occur only once in 1 to 3 million doses. He said that there is concern that IPV adverse effects could occur with severity and frequency equivalent to those from OPV, but without its benefits.

In addition, federal agency and private organization officials said that the availability of a vaccine is not usually a major consideration in deciding which vaccine to recommend for childhood immunization. These officials said that for most vaccines, including polio, manufacturers can produce a sufficient quantity of vaccine within a short period of time. The Immunization Practices Advisory Committee officials said that because vaccine manufacturers attend its meetings, manufacturers are aware that the vaccine is being considered for recommended use. Thus, when a recommendation is made, manufacturers can be ready in a relatively short period of time to supply the needed quantity of vaccine.

(108878)